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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/688,254	10/13/2000	Harry M. Meade	10275-139001	9900

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EXAMINER	
QIAN, CELINE X	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 02/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/688,254	MEADE ET AL.	
	Examiner	Art Unit	
	Celine X Qian	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8-10,12-15 and 19-30* is/are pending in the application.

4a) Of the above claim(s) *1-4 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,6,8-10,12-15 and 20-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-6, 8-10, 12-15 and 19-30 are pending in the application.

This Office Action is in response to the Amendment filed on 11/13/02.

Claim 7 is cancelled. Claims 1-4 and 19 are withdrawn from consideration for being directed to non-elected subject matter. Claims 5, 6, 8-10, 12-15 and 20-30 are under examination.

Election/Restrictions

Claims 1-4 and 19 are withdrawn from further consideration for being drawn to non-elected invention. Applicants elected the invention of Group I in paper no.9, which are drawn to a transgenic system for purification of a target polypeptide and a method of producing said polypeptide. Claims 1-4 and 19 are drawn to a purification system comprising milk, a target polypeptide and a matrix. Therefore, these claims are directed to non-elected invention.

Response to Amendment

Acknowledge is made of Applicants' submission of formal drawings.

The rejection of claims 1-4 and 15 under 35 U.S.C.101 has been withdrawn in light of Applicants' amendment of the claims.

The rejection of claims 1-4 under 35 U.S.C.112 1st paragraph is moot because the claims are withdrawn from consideration.

The rejection of claims 1-10 and 12-15 under 35 U.S.C.112 2nd paragraph has been withdrawn in light of Applicants' amendment of the claims.

Claims 20 and 26 are rejected under 35 U.S.C.112 1st paragraph (new matter) for reasons discussed below.

Claims 9, 10, 21, 22 and 28 are rejected under 35 U.S.C.112 1st paragraph (written description) for reasons discussed below.

Claim 25 is rejected under 35 U.S.C.112 2nd paragraph for reasons discussed below.

Claims 5, 6, 8-10, 12-15, 21-25, 27-30 rejected under 35 U.S.C. 103(a) for reasons discussed below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9, 10, 20-22, 26-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 20 and 26 recites "the transgenically produced multivalent polypeptide further comprises a third binding moiety..." There is no support in the specification for this third binding moiety. Therefore, the claims contain new matter.

The written description requirement is set forth by 35 U.S.C. 112, first paragraph which states that the: "*specification* shall contain a written description of the invention. . .[emphasis added]." The written description requirement has been well established and characterized in the case law. A specification must convey to one of skill in the art that "as of the filing date sought, [the inventor] was in possession of the invention." See *Vas Cath v. Mahurkar* 935 F.2d 1555,

1560 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). Applicant may show that he is in "possession" of the invention claimed by describing the invention with all of its claimed limitations "by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention." See *Lockwood v. American Airlines Inc.* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

Claims 9, 10, 21, 22, 27 and 28 recite "a functional fragment thereof" an antibody, a cellulose binding domain, or protein L. The specification does not describe any functional fragment of an antibody, a cellulose binding domain (CBD), or protein L. The specification also fails to describe the function of such antibody, cellulose binding domain or protein L. As such, it is unclear which part of the antibody, CBD or protein L is responsible for the claimed function. It is also unclear the size of the fragment or how many fragments that are responsible for the claimed function. Thus, the specification neither describes the invention by their complete structure nor by other relevant identifying characteristics. Therefore, the specification fails to describe the invention in such a way to convey one skilled in the art that the inventors had possession of the claimed invention at the time of filing.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 25 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "the transgenically...is produced in the milk of the non-human transgenic mammal" renders the claim indefinite because it is unclear whether the polypeptide is

produced in the milk of the same transgenic mammal which the target polypeptide is to be purified. If this is the case, it appears that it is unnecessary to contact the milk with the transgenically produced multivalent polypeptide because they are in the same milk. If the multivalent polypeptide is produced in another mammal, then this claim is same as claim 15. Appropriate clarification is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 5, 6, 8-10, 12-15, 21-25, 27-30 rejected under 35 U.S.C. 103(a) as being unpatentable over Cheng et al. (5,981,714), in view of Scharwz et al. (5,719,269), Radford et al. (5,955,270), Wagner et al. (6,329,209), Vola et al., (1994, Cell Biophysics 24/25, p.27-36 abstract), Meade et al. (5,750172), and Nuijens et al. (1997, JBC, Vol.272, No.13, pp.8802-8807).

Cheng et al. teach a method of purifying a target polypeptide by using antibody which binds to a matrix. Cheng et al. also teach that the standard method for such purification consists preparation of antibody-matrix, binding an antigen to the antibody-matrix, removing contaminants by washing, and elution of the antigen (see col. 7 line 56 through line 12, col. 8). However, Cheng et al. does not teach that the antibody is made transgenically. Cheng et al. do

not teach that the target polypeptide is an antibody. Cheng et al. do not teach that the antibody used to purify the polypeptide having either protein L or CBD. Cheng et al. do not teach that the target polypeptide is a receptor or a ligand.

Schwartz et al. teach that method of purifying an antibody by using immobilized ligand immobilized to a matrix is well known in the art (see col.1, 4th paragraph). Schwartz et al. also teach that bacterial protein A, G and L are commonly used in this method because they specifically bind to IgG antibodies (see col. 1 through col. 2, 2nd paragraph).

Radford et al. teach that by adding the cellulose binding domain to a expression construct makes it easier for the subsequent purification (col. 2 line 59 through col.3 lines 13). Radford et al. further teach a method of purifying cellobiohydrolase-1 comprising the cellulose binding domain can be used to bind to a cellulose matrix and washing off other components, thereby purifying said enzyme.

Wagner et al. teach that a method of capturing proteins to an array chip by using capturing agents that are attached to the chip (col.3). Wagner et al. also teach that the capturing agents can bind a protein to itself in a specific manner. They include antibodies, wherein the binding partner is antigen, and receptors, wherein their binding partner is ligand (see col.4, lines 48-67).

Vola et al. teach that bacterial protein L binds specifically to human kappa light chains and murine monoclonal IgG. Vola et al. teach that protein L can be used in the purification procedure of murine Igs (see abstract).

Nuijens et al. teach the expression and characterization of the recombinant human lactoferrin secreted in milk of transgenic mice. Nuijens et al. teach that the transgenically

produced lactoferrin is very similar to the natural lactoferrin, and exerts same anti-bacterial and anti-inflammatory activities in vivo.

Meade et al. teach the production of a number of recombinant proteins including TPA, urokinase, growth hormones and immunoglobulins in the milk of transgenic non-human mammal (see col.3, 3rd paragraph, and Examples 1-3).

Based on the combination of teaching of Cheng et al. (5,981,714), Scharwz et al. (5,719,269), and Nuijens et al. (1997, JBC, Vol.272, No.13, pp.8802-8807), it would have been obvious to one of ordinary skill in the art to develop a method of purifying target polypeptide either from milk of a transgenic mammal or other mixtures by contacting the target polypeptide with a transgenically produced multivalent binding polypeptide, (for example, the antibody that is capable of binding to a matrix taught by Cheng et al.) having a first bindable eptitope which binds the target polypeptide (for example, the antigen taught by Cheng et al.) and a second bindable eptitope which binds a matrix, and subsequent elution of the polypeptide from the matrix. The ordinary artisan would have been motivated to do so because a transgenically produced polypeptide is structurally same as the natural occurring polypeptide as demonstrated by Nuijen et al. Further, Meade et al. teach the generation of recombinant immunoglobulins in the milk of the transgenic non-human mammal. At the time of filing, the skill of art in producing recombinant protein in milk of transgenic mammal is high. Absent evidence to the contrary, one of ordinary skill in the art would have reasonable expectation of success to develop such a purification method using the multivalent polypeptide that is produced by a transgenic mammal. Therefore, the invention would have been *prima facie* obvious to one of ordinary skill of art at the time the invention was made.

It would also have been obvious to one of ordinary skill of art to use protein L as the first binding moiety or CBD as the second binding moiety of the multivalent polypeptide based on the teaching of Cheng et al. (5,981,714), Scharwz et al. (5,719,269), Radford et al. (5,955,270), Vola et al., (1994, Cell Biophysics 24/25, p.27-36 abstract) and Nuijens et al. (1997, JBC, Vol.272, No.13, pp.8802-8807). The ordinary artisan would have been motivated to do so because Vola et al. teach that L protein binds to Igs and is useful in purifying antibodies, and Radford et al. teach that CBD binds to cellulose matrix and makes it easier to purify proteins comprising this domain. Since the nucleic acid sequence encoding those binding domains are known, attaching them to a polypeptide would have been routine experimentation at the time of filing. Absent evidence from the contrary, the ordinary skill of art would have reasonable expectation of success to produce a multivalent polypeptide with protein L and/or CBD domain transgenically and use it to purify a target polypeptide such as IgGs. Therefore, the invention would have been *prima facie* obvious to one of ordinary skill of art at the time the invention was made.

It would also have been obvious to one of ordinary skill of art to use a receptor as the first binding moiety when the target polypeptide is a ligand or vice versa based on the teaching of Cheng et al. (5,981,714), Wagner et al. (6,329,209), and Nuijens et al. (1997, JBC, Vol.272, No.13, pp.8802-8807). One of ordinary skill of art would have been motivated to do so because Wagner et al. teach that receptor-ligand interaction is specific for protein capturing agent to bind to the ligand in a biological sample. Many receptor and ligand have been cloned and characterized at the time of filing. One ordinary skill of art would have plenty of information to choose receptor when a ligand needs to be purified and vice versa. Absent evidence from the contrary, one of ordinary skill of art would have reasonable expectation to transgenicIly produce

a multivalent polypeptide with a binding moiety either from a ligand or a receptor. Therefore, the invention would have been *prima facie* obvious to one of ordinary skill of art at the time the invention was made.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Celine Qian, Ph.D.
January 27, 2003

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER